**Master 2 internship project**

**Year 2024-2025**

**Laboratory/Institute:** Biosanté U1292 INSERM-CEA-UGA **Director:** Dr. A Andrieux

**Team:** MAB2 **Head of the team:** Dr N Alfaidy

**Name and status of the scientist in charge of the project:** Dr C. Marquette DR CEA **HDR: yes X** no **☐**

**Address:** 17 rue des martyrs, 38000 Grenoble / **Phone:** 04 38 78 37 65 **e-mail:** christel.marquette@cea.fr

**Program of the Master’s degree in Biology:**

**☐** Microbiology, Infectious Diseases and Immunology **☐** Structural Biology of Pathogens **☐** Physiology, Epigenetics, Differentiation, Cancer **X Neurosciences and Neurobiology**

**Title of the project: Impact of preeclampsia on cortical development**

**Objectives**: Investigate the dysregulated mechanisms of cortical development upon inflammatory preeclampsia context and their cognitive consequences.

**Abstract:** The major challenge in developmental biology is to understand how the brain is formed in normal and pathological conditions. Abnormal brain development in humans and mammals, particularly of the cerebral cortex, results in neurodevelopmental disorders (NDs) that are characterized by a combination of cognitive and/or motor symptoms and are associated with anatomical defects, known as malformations of cortical development. During pregnancy, cortical development can be affected by several factors including the fetal environment, as suggested in the context of preeclampsia (PE). PE, affecting 2–8% of pregnancies worldwide, is a multisystem disorder of pregnancy endangering the life of mother and fetus and characterized by chronic hypertension and significant proteinuria. This pathology arise from defective placentation, leading to placental hypoperfusion and abnormal fetal supply in oxygen and nutrients. In addition, numerous studies described an inflammatory response of placenta during PE, with a significant secretion of pro-inflammatory interleukins and oxidative factors. Importantly, there is growing evidence that children exposed to severe preeclamptic pregnancies have a higher risk of cognitive impairment and NDs. However, the causal relationship between placental dysfunction and cortical development defects has never been established.

Preliminary results obtained in pups at P2, P5 and P9, who grew up in preeclamptic mothers, indicate an alteration in corticogenesis and early communication behaviour.

**Methods:** During the internship, the candidate will study the impact of the PE condition at the embryonic stage on the architecture of the entire developing cortex, by analysing specific neuronal markers in the different cortical layers. Using in utero electroporation of embryos with a plasmid expressing green fluorescent protein (GFP), analysis of neuronal maturation, dendritic morphology and axonal projections in normal and PE cortexes will be assessed. To study these connections on a whole-brain scale, we will use the 3DISCO method to obtain 3D acquisitions for high spatial resolution explorations. The candidate will work in close collaboration with our research team and will perform immunofluorescence experiments and will be involved in the follow-up of animal experiments, including cross-breeding and genotyping.

**Relevant publications:**

Barnat et al. « Huntington’s disease alters human neurodevelopment ». Science, 2020, 369, no 6505: 787 93. <https://doi.org/10.1126/science.aax3338>.

Doridot et al.,« Preeclampsia-Like Symptoms Induced in Mice by Fetoplacental Expression of STOX1 Are Reversed by Aspirin Treatment ». Hypertension, 2013 61, no 3: 662 68. <https://doi.org/10.1161/HYPERTENSIONAHA.111.202994>

**Requested domains of expertise:** The candidate will be a highly motivated M2 student, with a background in neuroscience/immunohistology/biochemistry/animal experimentation, and strong analytical and organisational skills. He/she will be able to work both independently and as part of a collaborative team (work in collaboration with the institute of Neuroscience of Grenoble), with a good ability to interact with people. He/She will be interested in pursuing a PhD after the M2 internship.

**Interested candidates** should send their CV, a cover letter (detailing motivation, relevant experiences and availability), and contact information for at least one reference to Christel Marquette: christel.marquette@cea.fr by October 15th, 2024.